

IN THE CLAIMS

Please cancel claim 17 without prejudice.

Please amend claims 1, 4, 5-6, 18-20, 23 and 25 as indicated below.

Please add new claims 29-37.

The listing of claims below will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A functionalized heparin-binding protein comprising a heparin-binding protein and at least one ~~covalently bonded~~ sugar chain covalently bonded thereto, wherein the at least one sugar chain is selected from the group consisting of a sulfated polysaccharide, a glycosaminoglycan, and an O-linked sugar chain ~~combined with a sulfated polysaccharide or a glycosaminoglycan, an N-linked sugar chain combined with a sulfated polysaccharide or a glycosaminoglycan, and combinations thereof~~, wherein the ~~residual~~ activity of the heparin-binding protein is increased by adding the at least one covalently bonded sugar chain, wherein the heparin-binding protein comprises the amino acid sequence of SEQ ID NO: 1, 17, 19, 21, 23 or 29.

2. (Canceled)

3. (Currently Amended) The functionalized heparin-binding protein of claim 1, wherein the heparin-binding protein is a factor belonging to the FGF family.

4. (Currently Amended) The functionalized heparin-binding protein of claim 1, wherein the at least one sugar chain is covalently bonded through to a peptide, which is covalently bonded to the heparin-binding protein to which the at least one sugar chain is added.

5. (Currently Amended) The functionalized heparin-binding protein of claim 4, wherein the heparin binding protein comprising the at least one covalently bonded sugar chain comprises:

(a) a protein consisting of the amino acid sequence of SEQ ID NO: 1, 17, 19, 21, 23, or 29; or

(b) a protein which consists of the amino acid sequence of SEQ ID NO: 1, 17, 19, 21, 23, or 29 having a deletion, substitution, addition or modification of at least one amino acid, wherein the heparin-binding protein comprising at least one sugar chain has FGF activity and wherein the peptide to which the sugar chain is added comprises a proteoglycan core protein or a part thereof.

6. (Currently Amended) The functionalized heparin-binding protein of claim 1, wherein the at least one sugar chain is bonded to the heparin-binding protein at a site forming a turn in the secondary structure, ~~or at a site near one of the ends~~, or at a site at which addition of the sugar chain will not change the tertiary structure of said protein sufficiently to cause said protein to incur a loss of activity.

7-13. (Canceled)

14. (Currently Amended) A pharmaceutical composition containing the functionalized heparin-binding protein of any one of claims 1 or 3-6 as an active ingredient.

15-17. (Canceled)

18. (Currently Amended) A functionalized heparin-binding protein which comprises a heparin-binding protein functionalized by covalently bonding thereto at least one sugar chain, wherein the at least one sugar chain is covalently bonded through to a peptide, which is covalently bonded to the heparin-binding protein to which the sugar chain is added thereby increasing the residual activity of the heparin-binding protein, said at least one sugar chain selected from the group consisting of a sulfated polysaccharide, a glycosaminoglycan, and an O-linked sugar chain ~~combined with a sulfated polysaccharide or a glycosaminoglycan, or an N-linked sugar chain combined with a sulfated polysaccharide or a glycosaminoglycan, and combinations thereof~~, wherein the heparin-binding protein comprises the amino acid sequence of SEQ ID NO: 1, 17, 19, 21, 23 or 29.

19. (Currently Amended) A functionalized heparin-binding protein comprising a heparin-binding protein and a plurality of covalently bonded sugar chains covalently bonded thereto, wherein the sugar chains are selected from the group consisting of a sulfated polysaccharide, a

glycosaminoglycan, and an O-linked sugar chain combined with a sulfated polysaccharide or a glycosaminoglycan, an N-linked sugar chain combined with a sulfated polysaccharide or a glycosaminoglycan, and combinations thereof, wherein the sugar chains are covalently bonded through to a peptide, which is covalently bonded to the heparin-binding protein to which the sugar chains are added thereby increasing the residual activity of the heparin-binding protein, wherein the heparin-binding protein comprises the amino acid sequence of SEQ ID NO: 1, 17, 19, 21, 23 or 29.

20. (Currently Amended) A functionalized heparin-binding protein comprising a heparin-binding protein containing a peptide sequence to which at least one sugar chain is covalently bonded, wherein the at least one sugar chain heparin-binding protein is covalently bonded through to the peptide sequence to which the at least one sugar chain is added, thereby increasing the residual activity of the heparin-binding protein, said at least one sugar chain selected from the group consisting of a sulfated polysaccharide, a glycosaminoglycan, and an O-linked sugar chain combined with a sulfated polysaccharide or a glycosaminoglycan, or an N-linked sugar chain combined with a sulfated polysaccharide or a glycosaminoglycan, and combinations thereof, wherein the heparin-binding protein comprises the amino acid sequence of SEQ ID NO: 1, 17, 19, 21, 23 or 29.

21. (Currently Amended) The functionalized heparin-binding protein of claim 20, wherein the heparin-binding protein is a factor belonging to the FGF family.

22. (Canceled)

23. (Currently Amended) A functionalized heparin-binding protein which comprises a heparin-binding protein modified with covalently bonded sugar chains, the sugar chain being selected from the group consisting of a sulfated polysaccharide, a glycosaminoglycan, and an O-linked sugar chain combined with a sulfated polysaccharide or a glycosaminoglycan, an N-linked sugar chain combined with a sulfated polysaccharide or a glycosaminoglycan and combinations thereof, wherein the activity of the heparin-binding protein is greater than the activity of the unmodified protein has improved stability over the unmodified proteins, wherein the heparin-binding protein comprises the amino acid sequence of SEQ ID NO: 1, 17, 19, 21, 23 or 29.

24. (Currently Amended) The functionalized heparin-binding protein of claim 1, wherein the at least one sugar chain is heparan sulfate.
25. (Currently Amended) The functionalized heparin-binding protein of ~~claim 16~~ claim 23, wherein the ~~at least one~~ sugar chain is heparan sulfate.
26. (Currently Amended) The functionalized heparin-binding protein of claim 18, wherein the at least one sugar chain is heparan sulfate.
27. (Currently Amended) The functionalized heparin-binding protein of claim 19, wherein the at least one sugar chain is heparan sulfate.
28. (Currently Amended) The functionalized heparin-binding protein of claim 20, wherein the at least one sugar chain is heparan sulfate.
29. (New) The functionalized heparin-binding protein of claim 23, wherein the stability is chosen from among the group consisting of thermostability, acid resistance, alkalai resistance and resistance to proteolytic enzymes.
30. (New) A functionalized heparin-binding protein comprising a heparin-binding protein and at least one sugar chain covalently bonded thereto,
said at least one covalently bonded sugar chain being selected from the group consisting of a sulfated polysaccharide, a glycosaminoglycan and an O-linked sugar chain,
said heparin-binding protein comprising (a) a proteoglycan core protein or a part thereof, to which said sugar chain is bonded, and (b) an amino acid sequence chosen from the group consisting of: the portion of the amino acid sequence of SEQ ID NO: 1 starting with Asn at number 88 and ending with Asp at number 221, the portion of the amino acid sequence of SEQ ID NO: 17 starting with Asn at number 67 and ending with Asp at number 200, the portion of the amino acid sequence of SEQ ID NO: 19 starting with Asn at number 67 and ending with Asp at number 200, the portion of the amino acid sequence of SEQ ID NO: 21 starting with Asn at number 121 and ending with Asp at number 254, and the portion of the amino acid sequence of SEQ ID NO: 23 starting with Asn at number 148 and ending with Asp at number 281,

wherein the activity of the heparin-binding protein is increased by adding the at least one covalently bonded sugar chain.

31. (New) The functionalized heparin-binding protein of claim 30, wherein the heparin-binding protein is a factor belonging to the FGF family.
32. (New) The functionalized heparin-binding protein of claim 31, wherein the heparin-binding protein is FGF-1 alpha.
33. (New) The functionalized heparin-binding protein of claim 30, wherein the heparin-binding protein comprising at least one sugar chain has FGF activity.
34. (New) The functionalized heparin-binding protein of claim 30, wherein the at least one sugar chain is heparan sulfate.
35. (New) The functionalized heparin-binding protein of claim 30, wherein the functionalized heparin-binding protein has improved stability over an unmodified heparin-binding protein.
36. (New) The functionalized heparin-binding protein of claim 35, wherein the stability is chosen from among the group consisting of thermostability, acid resistance, alkalai resistance and resistance to proteolytic enzymes.
37. (New) A pharmaceutical composition containing the functionalized heparin-binding protein of claim 30 as an active ingredient.